Non-technical Abstract

In animal models, regression of several types of tumors following administration of recombinant IL-2 protein (Interleukin 2) or adenoviral vectors expressing IL-2 has been reported. IL-2 is effective because it promotes an anti-tumor immune response.

GENEMEDICINE, INC. has developed a non-viral gene therapy that produces hIL-2. It is anticipated that this product will promote tumor regression, inhibition of progression, and/or prevention of metastasis when given for the treatment of squamous cell carcinoma of the head and neck. Data from rodent tumor models support this hypothesis. Intratumoral administration of the hIL-2 Gene Medicine results in an increase in the levels of IL-12 and γ-IFN, two cytokines which are known to contribute to an anti-tumor immune response. When administered intratumorally to tumor-bearing mice, hIL-2 Gene Medicine slows tumor growth. These data suggest that administration of the formulated hIL-2 plasmid also will lead to the generation of an anti-tumor immune response and subsequent tumor regression, inhibition in tumor progression, and/or prevention of metastasis in humans.

The ability of recombinant IL-2 protein to induce an anti-tumor immune response is documented. However, in order to achieve effective levels of IL-2 in the tumor, high doses of the recombinant protein have been administered intravenously. These high doses of recombinant protein have serious side-effects. The proposed project is directed at expressing human IL-2 in the tumor by liposome-mediated delivery of a therapeutic gene encoding IL-2. This gene therapy will induce local (tumoral) expression of IL-2 to induce an anti-tumor response without producing high concentrations of IL-2 throughout the body. This offers a distinct advantage since the likelihood of occurrence of side-effects from high doses of IL-2 should be greatly reduced, if not eliminated. In addition, the IL-2 protein lasts in the blood for only 6-10 minutes, thereby requiring multiple administrations for optimal effect. IL-2 gene therapy is expected to produce protein in the tumor for days, obviating the need for multiple administrations. Finally, liposome-mediated DNA delivery does not utilize a recombinant virus for delivery of the therapeutic gene, thereby eliminating potential side-effects associated with virus exposure.

This Phase I trial is designed to evaluate the safety of hIL-2 Gene Medicine in humans. Each patient will receive a single intratumoral injection of formulated hIL-2 plasmid or vehicle. Physical examinations and evaluations of clinical chemistry and hematology will be conducted to assess safety and tolerability. In addition, DNA analysis and immunohistological studies will be performed with tissue obtained by biopsy to evaluate expression of the IL-2 gene and stimulation of the immune system.